Annals of the New York Academy of Science

PART III. BACTERIA AS AGENTS OF AIRBORNE CONTAGION

INHALATION ANTHRAX

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INTRODUCTION

Inhalation anthrax, now primarily only of historical interest, remains an intriguing disease. When the rare case occurs, it raises epidemiologic questions that are difficult to answer.

At the Second International Conference on Aerobiology in 1966,[1] I reported in detail on a field experiment designed to study some of the clinical and epidemiologic features of this disease. In the study we exposed 91 cynomolgus monkeys (*Macaca fascicularis*) to naturally occurring aerosols containing *Bacillus anthracis* in a goat-hair-processing mill; the resultant anthrax mortality rate was 25.3%. I discussed the pathologic findings and the dose-response relationships resulting from what in effect was chronic exposure to *B. anthracis.*

Today, I will briefly review the 18 cases of inhalation anthrax in humans that have been reported in the United States since 1900 and summarize a few of the more recent cases to point up some of the epidemiologic details of inhalation anthrax as currently seen in the Untied States.

Historical Aspects

The history of anthrax began in biblical times with one of the so-called great plagues, which is believed to have been anthrax. Inhalation anthrax was not specifically described, however, until the mid-1800s, when it was recognized as a significant problem among British woolsorters who worked in the textile industry, especially those employed in Bradford, England.[2] In 1837, mohair (a type of goat hair) from Asia Minor and alpaca from Peru were first introduced into the developing Bradford textile industry. Soon after, a mysterious and rapidly fatal illness began to occur among the sorters, who because they primarily sorted wool were known as wool sorters, and the disease was referred to as woolsorters' disease. However, the disease was the result of contact not with wool, but with goat hair or alpaca. A similar disease, though not as common, began to be seen in Germany in persons who handled rags, and the disease was known as ragpickers' disease.

From 1847 to 1877, as woolsorters' disease became more prominent, information accumulated concerning its clinical pattern, virulence and association with imported goat hair and alpaca. Workers became selective as to what batches of mohair they would sort.

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

In the late 1870s, Bell[3] studied inhalation anthrax among textile workers; he identified the organisms in the blood, which he used to transmit the disease by inoculation into mice and rabbits. To prevent the occurrence of the disease, Bell recommended that manufacturers wash potentially dangerous material before having it sorted, an action adopted by some manufacturers.

In 1880 a coroner's jury, having investigated one publicized death due to inhalation anthrax, recommended that bales of hair be steeped in salt water for not less than 12 hours and that they be washed at least twice in water at a temperature of 120° before being sorted.[2] They also made recommendations concerning ventilation and methods of cleaning work areas. These recommendations were put into effect in the early 1880's, which led to a decrease in the number of cases of woolsorters' disease.

An Anthrax Investigation Board for Bradford and District was formed in 1905[4] to further study the problem and make additional recommendations. A bacteriologist, F. W. Eurich, was appointed to classify materials according to the degree of risk of anthrax and to carry out experiments as to the practicality of lowering the risk of disease following manipulation of certain classes of wool and hair.

Over the past 20 years, Eurich processed 200,000 cultures and bacteriologically analyzed more than 14,000 specimens of alpaca, mohair and wool. His investigations demonstrated that the presence of *B. anthracis* was associated with the "general dirtiness" and blood contamination of the fibers. He classified goat hair from East India, Persia, and Turkey as the most heavily contaminated and evaluated the effectiveness of hot water, dry heat, formaldehyde, formalin gas, white wash, disinfectants, and several other compounds in killing spores. Eurich found that formaldehyde appeared to be the best disinfectant; in cooperation with an inspector of factories he developed a method of washing the fibers with an alkaline solution and formaldehyde. This destroyed anthrax spores in goat hair.

The Anthrax Prevention Act of 1919 stated that mohair, raw wool, and alpaca from specific areas could be imported into Great Britain but they had to be decontaminated at the government Wool Disinfection Station in Liverpool, which opened in 1921, before being processed.[2] Subsequently, inhalation anthrax was seen at a significantly lower rate among woolsorters; no cases have been reported since 1939.

Eurich also noted that there might be some relationship between woolsorters' disease and certain chronic health conditions, such as alcoholism, which I will comment on later.

One additional point of interest is that the Anthrax Investigation Board noted in 1918 that there was worldwide interest in inhalation anthrax and hoped "that the assistance of the United States in the war with anthrax would be as useful and effective as the aid had so effectively rendered to the Allied cause in the great conflict just ended."[5]

Clinical Aspects

Before reviewing the occurrence of inhalation anthrax in the United States, let me first briefly summarize its clinical aspects. The classic clinical picture is that of a biphasic disease. The initial stage consists of the insidious onset of mild fever, malaise, fatigue, myalgia, nonproductive cough, and at times a sensation of precordial oppression.[6] There are few objective

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

findings aside from fever. Rhonchi may be heard on auscultation of the lungs. This initial phase typically lasts for several days, following which there may be some improvement in the clinical condition.

The second stage develops suddenly with the onset of acute dyspnea and subsequent cyanosis. The patient may appear moribund with accelerated pulse and respiration rate. The body temperature may be mildly elevated, or it may be subnormal because of shock. Stridor may occur perhaps as a result of partial extrinsic obstruction of the trachea by enlarged mediastinum nodes. Profuse perspiration is frequently present. Physical examination of the chest reveals moist, crepitant rales and signs of pleural effusion. Consciousness typically is maintained until death, but with meningeal involvement there may be disorientation, coma, and meningismus. A chest roentgenogram typically shows widening of the mediastinum. The average duration of the acute stage is less than 24 hours, which almost always ends in death.

Diagnosis of inhalation anthrax during the first stage is difficult since the signs and symptoms are that of a mild respiratory disease, and frequently the diagnosis is a "cold," influenza, or bronchitis. In the second stage the diagnosis is frequently cardiac failure or a cardiovascular accident. Though blood cultures may be positive in the acute phase, death usually ensues before the organism can be identified.

Pathogenesis

Historically, there were two theories on the pathogenesis of inhalation anthrax.[7] One was that the inhaled spores are phagocytosed by macrophages and transported through the alveoli to the mediastinum, where germination occurred and toxin was produced by the vegetative cells.[8] The other theory was "that the primary lesion was an erosion of the tracheobronchial mucosa (similar to a cutaneous lesion) usually occurring near the point of bifurcation," and that pneumonia developed secondary to the initial point of entry.[9] Buchner[10] in 1888 infected rabbits, guinea pigs, and mice with clouds of *B. anthracis* spores and took sections of the lungs at intervals after exposure, but was unable to demonstrate the site of germination of the spores. In the 1940s Young, Zelle, and Lincoln[11] and Barnes[12] exposed animals to clouds of *B. anthracis* spores in the laboratory and determined that involvement of the pulmonary tissue was secondary to the systemic disease but were unable to determine the original site of invasion of the spores and the exact method by which they were transported. Druett, Henderson, Packman, and Peacock[13] exposed guinea pigs and monkeys to clouds of homogenous particles containing *B. anthracis* spores and surmised that infection of the animals occurred most effectively following inhalation of single spores approximately 1 micron in diameter, though with particles up to a diameter of 5 microns there was only slightly less effectiveness. With particles larger than 5 microns, there was a remarkedly rapid fall off in infectivity. Ross instilled liquid suspensions of *B. anthracis* spores intratracheally in guinea pigs and serially examined the tissues from these animals; he thus demonstrated that the spores were usually phagocytized within a matter of minutes by macrophages present in the alveoli, transported across the alveolar membrane and carried by the draining lymphatics, into the sinusoids of the lymph nodes where germination of the spores occurred with development of vegetative forms.[14] When the vegetative forms escaped

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

from the macrophages, rapid multiplication occurred, and the bacilli were disseminated throughout the tissue. The toxin causes hemorrhage, edema, and necrosis. Since the organisms are initially localized in the mediastinal nodes, the initial and major site of involvement is the mediastinum; toxin causes massive hemorrhagic mediastinitis, which is typical of inhalation anthrax. Once a sufficient level of toxin has been reached, death almost invariably follows despite sterilization of the vascular system by antibiotics. It is clear that without preexisting pulmonary disease no true primary respiratory infection develops; secondary pneumonia has been reported.

Another acute-exposure study that added to our knowledge about inhalation anthrax was performed by Albrink and Goodlow,[15] who exposed chimpanzees to clouds of *B. anthracis* spores. When two animals were exposed to 35,000 spores, they had blood cultures positive for *B. anthracis* but no evidence of clinical disease. Two other chimpanzees were exposed to 40,000 and 65,000 spores respectively; both developed bacteremia on the first or second postexposure day and died on the sixth postexposure day. The animals appeared to be normal until approximately 4-7 hours before death and died on the eighth postexposure day. At autopsy, there was no evidence of pneumonia, but acute hemorrhagic mediastinitis with edema in the mediastinal area was present. The architecture of the tracheobronchial lymph nodes and others in the mediastinal area was obliterated by hemorrhage.

Inhalation Anthrax in the United States

In the United States, only 5% of anthrax cases are inhalation anthrax, the rest are cutaneous; gastrointestinal cases have never been reported here.[18] Eighteen cases of inhalation anthrax have been reported in the American literature since 1900. (TABLE 1) Sixteen were fatal. Ten of the cases occurred sporadically. Three of the cases that occurred over a 10-year span may have been associated with one tannery, and five of the cases that occurred over a 10-week period were part of an epidemic at one goat-hair-processing mill.[17] All of the inhalation cases were related to industrial sources of infection (except the two laboratory-associated cases); whereas 78% of the cutaneous cases were industry related and 22% agricultural.

Analysis of the type of industrial contact in the inhalation cases is shown also in TABLE 1; 10 patients had direct contact with the industrial source, and three had indirect contact (one patient was a home craftsman and two had laboratory contact). In two cases the source of infection was unknown. TABLE 2 compares the source of infection of inhalation and cutaneous industrial cases; the similarities can be seen.

Case Reports

To illustrate some of the clinical and epidemiologic features and protean aspects of inhalation anthrax, I will review a few cases that have been investigated.

The first case represents a patient who had no known predisposing ill health conditions and who had only brief exposure to contaminated aerosols. In 1961, a 51-year-old woman in good

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

TABLE 1

18 CASES OF INHALATION ANTHRAX, BY INDUSTRIAL CONTACT, UNITED STATES 1900-1978

Industry (goat hair/skins or sheep wool/skins)	
Direct	10
Indirect	3
Home Craftsman	1
Laboratory	2
Unknown	2
Total	18

TABLE 2

INDUSTRIAL HUMAN ANTHRAX CASES, UNITED STATES BY SOURCES OF INFECTION 1900-1978

	Inhalation 1900-1978		Total 1955-1978	
Source of Infection	Number	Percent	Number	Percent
Goat Hair	9	53	112	62
Goat Skins	2	12	16	9
Goat Hair or Skins	1	6	--	--
Wool	1	6	34	19
Tannery	1	6	--	--
Meat, Bones	--	--	8	4
Rugs	1	6	--	--
Laboratory	2	6	--	--
Unknown	1	6	11	6
Total	18	101	181	100

health reported weakness, chills, a nonproductive cough, and a dull chest pain, which eventually became constant, in her substernal area. Her physician diagnosed this as a viral illness. The following day her condition became worse, with generalized aches, abdominal pain, temperature of 102°F, and she was hospitalized. On physical examination, she had occasional bilateral wheezes over the lungs. Her white blood cell count was 13,100/mm^3. A chest roentgenogram revealed obliteration of the left hemidiaphragm and costophrenic angle with moderate prominence of the left hilar region. That evening she became cyanotic, and the following morning she went into shock and died.

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

At autopsy, she had pleural effusion, classic hemorrhagic edematous mediastinitis as seen in inhalation anthrax, and acute splenitis.

The textile mill where she worked processed imported goat hair. Prior to a company-wide vaccination program in 1957, the mill had reported one case of cutaneous anthrax per 100 mill employees per year and had never reported a case of inhalation anthrax. The patient had never been vaccinated against anthrax. She worked in an office next to an equipment storage area. She occasionally handled samples of the finished product but only infrequently handled samples of raw goat hair. Rarely did she walk into the mill, but on the day preceding the onset of her illness she did visit the carding room, a relatively dusty environment where raw hair is handled. An environmental sampling program after she died revealed gross contamination of the raw goat hair being processed as well as of the mill itself.

The most recent reported case of inhalation anthrax in the United States occurred in 1976 and involved a 32-year-old home craftsman.[18] Five days before being hospitalized he began complaining of fever and a sore throat. During the next five days his complaints included left-sided chest pains, headaches, nausea, and anorexia. Physical examination at the time of admission revealed an acutely ill patient with decreased breath sounds over the left lower lung field. Neurologic examination demonstrated an inability to carry out simple commands, left upper and lower extremity spasticity, disconjugate gaze, and intact tendon reflexes. X-ray examination of the chest displayed a moderate-size left pleural effusion and enlargement of the left pulmonary hilus. The cerebrospinal fluid protein was 220 mg/dl and glucose 65 mg/dl. Large gram-positive rods were seen in the spinal fluid and in the left pleural effusion fluid. The patient was treated with intravenous penicillin and intramuscular streptomycin, but died 28 hours after admission.

The autopsy revealed classic evidence of inhalation anthrax and, in addition, subarachnoid hemorrhage. A small chromophobe adenoma of the pituitary gland was present.

The patient was a self-employed artistic weaver who worked in his own with yarn obtained from commercial sources. The yarn he was working with had been imported from Pakistan and contained various animal fibers. It was cultured and found to be positive for *B. anthracis.*

These two cases represent individuals with no known predisposing conditions as related to developing inhalation anthrax. Their exposures were brief and at least in the last case unusual.

This next case raises a question concerning the association between several potential predisposing health factors and inhalation anthrax in an individual with only sporadic exposure to *B. anthracis.*

The patient, a 53-year-old man, had been employed in a biological laboratory as an electrician for six years before his terminal illness. His work took him into many buildings where various laboratory activities were in process. He had had some contact with beryllium but not in excess of that experienced by his coworkers. In 1957 laryngeal carcinoma *in situ* was noted and removed. In May 1958, two months before his terminal illness, a routine physical examination including a chest roentgenogram was negative. Two weeks before the onset of his terminal illness, he received yellow fever, tularemia, and small pox vaccines and a brucellosis skin test. He had never received anthrax vaccine.

On June 29, 1958, he experienced the abrupt onset of fever, headache, and muscle aches, and on the following day was admitted to a hospital, where his rectal temperature was 103.6°F. He was not acutely ill. The white blood cell count was 8,100/mm^3 with 84% neutrophils. A

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chest film revealed symmetrical widening of the upper mediastinum, apical capping, and a focal area of consolidation in the right mid-lung field.

On the day after admission, his white count had risen to 15,000/mm^3 and repeat roentgenograms showed linear atelectasis in the left lower lobe and fluid in the left base. He was started on intravenous tetracycline, 2 grams a day.

During the following several days he developed a slight cough, bilateral pleural effusion, and tachycardia; his blood cultures were positive for *B. anthracis*. On the sixth day of his disease he was cyanotic and developed expiratory wheezes over the right lung; roentgenograms showed focal areas of density throughout the lung field, and bilateral pleural fluid; the mediastinal widening persisted. He became more restless and apprehensive; his breathing became labored and he expired on the same day.

A significant difference between this case and the previous cases was the more graduate development of the acute phase without any evidence of improvement between the two phases of the disease.

At autopsy, the principal pathologic findings were those of edematous, hemorrhagic mediastinitis as seen in inhalation anthrax. A hemorrhagic area in the middle lobe of the right lung was present, and beryllium was found in trace amounts in the same area. Old fibrotic and calcific changes in the pulmonary tissues associated with anthracosis were noted and were felt to be the cause of some lymphatic obstruction. Additionally, there were some minor anatomic abnormalities of the upper respiratory passage.

Environmental culturing in buildings in which he had worked during the two weeks prior to his terminal illness revealed *B. anthracis* organisms in small numbers in three of the eight buildings; organisms were recovered from the surface of his tool pouch.

It is hypothesized that he was exposed to *B. anthracis* spores while working in one of the buildings in which *B. anthracis* spores had been previously handled. He had inhaled The organisms through an upper respiratory tract with some minor anatomical abnormalities that may have reduced the effectiveness of the filtering mechanism. Because of the multiple immunization procedures two weeks prior to his illness, his resistance to a new infection may have been reduced. In addition to generalized toxemia, because of the defective pulmonary tissue (old fibrosis) and the focus of beryllium involvement in one lung, secondary pulmonary changes developed.

The next case portrays another individual with several compromising health conditions, but only peripheral and probably brief contact with *B. anthracis*.[18] The patient, a 46-year-old man with a history of alcoholism, recurrent pancreatitis, and diabetes, had worked in a metal fabricator shop for only three weeks when the plant closed for a 2-week summer vacation. Six days later he was found mildly intoxicated and complaining of fatigue. For the next two days he was tremulous, but this was attributed to his alcoholic indulgence. On the following day, or three days after the onset of symptoms, he appeared to have improved, he was alert, and only a chronic cough persisted. One day later he fell out of bed and was noted by his wife to be confused, lethargic, and perspiring. His family physician found him to be unresponsive, perspiring, and cold with shallow respirations. He was taken to a local hospital.

Pertinent physical findings included loud tracheal gurgling and bilateral basilar pulmonary rales. A chest roentgenogram revealed a paratracheal mass, basilar pneumonia, and pleural

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

effusion on the right side. He had a hematocrit of 50 percent and a white blood cell count of 15,800/mm^3 with 50 percent neutrophils and 41 percent band forms.

The patient was treated with insulin, intravenous fluid, chloramphenicol and penicillin. He became hypotensive, was refactory to pressor agents, and died six hours after admission.

At autopsy, the mediastinum and mediastinal lymph nodes were hemorrhagic and edematous as seen in inhalation anthrax. There was 1500 cc of bloody right pleural effusion. The pulmonary parenchyma was congested, but there were no areas of consolidation. Microscopically, the brain was covered with diffuse hemorrhagic leptomeninigitis, and the lungs were congested, with patchy areas of focal hemorrhage. Large gram-positive bacilli were seen in the mediastinal lymph nodes, meninges, and lungs. *Bacillus anthracis* was recovered from the hemorrhagic mediastinal lymph nodes. The epidemiologic investigation revealed that the metal fabricating plant in which the patient and 35 other employees worked was located across a 60-foot alley from the building that housed the goat-hair-processing mill associated with the 1957 epidemic of inhalation anthrax. In the period from January 1941 to June 1957 the mill had reported 136 cases of cutaneous anthrax, or 8.2% cases per year. Following the epidemic of inhalation anthrax in 1957, all employees had been vaccinated. During the 10 years following vaccination, only four cases of cutaneous anthrax or 0.4 cases per year, had been reported. The source of goat hair remained unchanged. The dustiest operations involved in processing the imported goat hair were performed in the corner of the mill closest to the metal fabricating shop. This operation created heavy aerosols that could be discharged into the alley by means of 2 window exhaust fans and through open doors and windows facing the alley.

Six months after the case occurred, an environmental sampling program was conducted. In the mill, *B. anthracis* was recovered from 25% of the gross samples of hair obtained from unopened bales and from 70(14.3%) of 489 surface swabs taken in the mill building. Twenty-five percent of the specimens obtained in the early-processing areas (those nearest the metal fabricating plant) were positive for *B. anthracis*, whereas only 6.2% of the swabs taken from the remaining processing areas were positive. In the picking area, 1,190 liters of air were sampled, and three isolations of *B. anthracis* were made. Assuming a constant exposure, a worker breathing at a rate of 7 cubic meters per eight hours would inhale approximately 200 spores of *B. anthracis* particles, less than 5 microns in size.

A total of 150 surface swabs were taken at the metal fabricating plant subsequent to renovation of the plant. Three of the swabs were positive for *B. anthracis*.

The epidemiologic and laboratory studies clearly revealed the opportunities for aerosol spread of *B. anthracis* from the mill into the alley and subsequently into the metal fabrication plant building. The workers confirmed that they often saw clouds of dust emanating from the open doors and windows of the picking and blending area of the mill. The patient worked in one end of the metal fabricating shop about 300 feet from the most contaminated area of the mill; however, on the last afternoon prior to vacation (six days before he became ill) the patient had worked for three to four hours in the alley directly opposite the picking and blending area. Weather records recorded temperatures in the 80s on this day with no rain showers during the work day. The windows and doors of the mill building would have been opened under these conditions.

The clinical course and pathologic findings confirmed the diagnosis of the inhalation anthrax. The projected incubation period of six days resembled those of previous cases. We do

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

not know whether chronic alcoholism, diabetes, and chronic pancreatitis could have predisposed the patient to inhalation anthrax.

The next case is that of a young man with chronic disease, sarcoidosis, who developed inhalation anthrax. The patient was a 28-year-old-man with a $2^{1/2}$-year-old, biopsy-proven history of sarcoidosis.[20] In April 1957, he gave a one-week history of increasing dyspnea, frequent coughing, and weight loss of seven pounds. Chest x-rays were similar to previous films. He was given prednisolone, 5 mg every four hours, of which he probably took two or three tablets that day. In the afternoon of the same day, he had severe substernal chest pains, and shortness of breath, was anorectic, and became restless. He was given penicillin, but within the next several hours his restlessness and dyspnea increased, and he produced a cupful of pink-streaked sputum.

He was admitted to a hospital early the following day in acute distress, complaining of chest pains, hemoptysis, and severe dyspnea. On physical examination, his respirations were 60 per minute, and he was cyanotic. Moist rales were heard over both lung fields. He was given morphine for sedation but subsequently coughed up bright red watery material, and died one hour after admission.

The pathologic findings were those of generalized sarcoidosis, inhalation anthrax, *B. anthracis* septicemia, and acute necrotizing pneumonia.

The one-week history of illness may have resulted from a recrudescence of sarcoidosis or a bacterial or viral pneumonia secondary to sarcoidosis. Either situation may have predisposed him to infection with *B. anthracis.* Possibly the week long illness represented inhalation anthrax, with its usual course retarded by the previous involvement with sarcoidosis. The development of acute necrotizing pneumonia may have been related to the impairment of the normal removal of *B. anthracis* organisms by sarcoidosis involvement of the lungs so that the retained organisms developed into the vegetative state within the alveoli cells resulting in focal, necrotizing pneumonitis. Additionally, pyogenic organisms may have been present initially but not revealed by postmortem cultures, so the autopsy findings may have resulted from the combined effects of sarcoidosis, *B. anthracis*, and septic pneumonia.

Gross examination as well as selected environmental culturing of a wooden furniture-frame manufacturing plant and a furniture store where he worked and his home revealed no sources of *B. anthracis.*

The most likely source of infection appeared to be the open receiving area of a tannery he walked past daily on his way to the bus stop where he caught a bus that took him home. He was never known to have gone inside the plant and had no acquaintances among the employees. *Bacillus anthracis* was isolated from 10 of 147 swabs (7%) obtained in the area of the tannery's receiving room six weeks after the patient's death. Three floor-sweeping specimens were positive for *B. anthracis.* No cases of inhalation anthrax had been reported among the employees of the plant, although a case of cutaneous anthrax had been reported in 1945. It was observed that the air currents blew from the tannery receiving area onto the street in the specific area where he walked.

Of interest are two other cases of inhalation anthrax also possibly related to the same tannery. One case was in a 50-year-old woman who in December 1948 complained of a "slight cold".[20] The next day she was better, but on the following evening she vomited, and early the next morning she complained of a headache and four hours later was found comatose. A

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

physician diagnosed acute meningitis, administered penicillin, and hospitalized her. Physical examination revealed the woman to be cold and clammy and cyanotic with severe respiratory distress with a rectal temperature of 105°F. Noisy breathing obscured auscultation of the cardiac and pulmonary sounds. The neck was rigid and there was flaccid paralysis of the extremities with hyperactive deep tendon reflexes. The white blood count was 14,800/mm^3 with 74% neutrophils and the cerebrospinal fluid was bloody. She died six hours after admission. Subsequently, the cerebrospinal fluid cultures were reported positive for *B. anthracis.* Pathologic findings were of hemorrhagic mediastinitis and subarachnoid hemorrhage. Gram-positive bacilli were seen in the blood vessels of the brain in the area of the subarachnoid hemorrhage. This woman, who was a housewife, lived one and one-half blocks from the tannery; no epidemiologic investigations were conducted at the time of her illness.

The other case possibly related to the same tannery was in a 37-year-old housewife with inhalation anthrax in 1951.[20] She lived one and one-half miles from the tannery and also 200 yards from a plant that processed waste wool and hair. No epidemiologic studies were conducted, so the possible association with the tannery can only be speculative. It is hypothesized that all three individuals may have become infected by the airborne route from the tannery, which was shown to be contaminated with *B. anthracis.*

As we stated at the 1966 Second International Conference on Aerobiology, "It is not clear why more cases have not occurred in goat hair and woolen mills and in tanneries, especially among employees working in the dustiest areas where the most concentrated *Bacillus anthracis*-containing aerosols were created." We suggested that the reason may be related to the dose to which employees are exposed, that resistance might develop among the employees with chronic exposure, or that more cases may have occurred but not have been diagnosed. We also stated that " equally unusual has been the sporadic occurrence of cases in people with no industrial exposure. It may be that these individuals are unusually susceptible …"

Reviewing the 18 cases in the United States since 1900 does not add any new information that answers these questions. The various studies conducted over the past 25 years, both in the laboratory and of naturally occurring aerosols in industrial plants where imported goat hair is processed, confirmed that the experimental disease in primates is similar to the disease in humans naturally exposed to industrial aerosols. The critical question concerning the infective dose for humans remains difficult to answer, and inferences can only be speculative. Although the human industrial case may reflect an unusually large dose of organisms, the influence of other factors, such as the possible role of potentiating substances also contained within the aerosol, or a highly virulent strain of *B. anthracis* are unknown. A few of the strains recovered from these patients have been studied in the laboratory. However, they do not appear to have any characteristics significantly different from typical strains.

The other area of concern, the health status of the host, may be related to the development of inhalation anthrax in at least some of the sporadic cases. The influence of a chronic disease on the subsequent development of inhalation anthrax was first mentioned in the reports of the Anthrax Investigation Board in England.

In at least three of the cases reviewed above, the individuals had chronic disease conditions that could have influenced their susceptibility. One of these individuals had berylliosis and potentially a compromised immune system, in addition to anatomic abnormalities of the upper respiratory tract. Another had chronic alcoholism, diabetes, chronic pancreatitis; the third had

Original Citation Published in: Annals New York Academy of Sciences Volume 353 Pages 83-93

chronic sarcoidosis. In several of the other cases, information is not adequate to show whether a chronic disease may have influenced the development of inhalation anthrax.

The five epidemic cases are easier to explain in that each of the patients were exposed to aerosols created by one particular lot of imported goat hair as it was being processed. Investigation revealed that the hair in this particular lot was heavily contaminated with *B. anthracis* and thus could have represented a common source of infection as it was being processed. It is possible that this lot may have been heavily contaminated. Except for the possibility that three cases were related to a single tannery, none of the other cases are related to each other or to a common source.

As we stated in the 1966 conference, " More specific information about inhalation anthrax in man is currently difficult to obtain because almost all workers in high-risk industries within the United States have been immunized." Additionally, during the past 13 years because of decreased importation and use of goat hair, the decrease in the number of workers working with the imported materials, the routine use of a human anthrax vaccine, and improvements in industrial hygiene, there has been a further reduction in the occurrence of this already rare disease. Thus, we should not look to additional field studies to provide new information that might answer the questions raised above. We can only assume that sporadic cases occur because individuals with greater susceptibility to infectious diseases are exposed to aerosols containing *B. anthracis* organisms, either in excessively high concentration or of unusual virulence.

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